UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

IN RE: TAXOTERE (DOCETAXEL) PRODUCTS LIABILITY LITIGATION	))))	**MDL No. 16-2740** **SECTION: "H" (5)**
This document relates to: Barbara Earnest, 16-17144	))	

ORDER AND REASONS

Before the Court is a Motion to Exclude Expert Testimony of David A. Kessler, M.D., J.D. (Doc. 6146) filed by Defendants Sanofi-Aventis U.S. LLC and Sanofi U.S. Services, Inc. (collectively, "Sanofi" or "Defendants"). The Court held oral argument on the Motion on July 25, 2019. For the following reasons, the Motion is **GRANTED IN PART**, **DENIED IN PART**, and **DEFERRED IN PART**.

BACKGROUND

Plaintiffs in this multidistrict litigation ("MDL") are suing several pharmaceutical companies that manufactured and/or distributed a chemotherapy drug, Taxotere or docetaxel,[1] that Plaintiffs were administered for the treatment of breast cancer or other forms of cancer. Plaintiffs allege that the drug caused permanent alopecia—in other words, permanent hair loss. Plaintiffs bring claims of failure to warn, negligent misrepresentation, fraudulent misrepresentation, and more.

[1] Docetaxel is the generic version of Taxotere.

The first bellwether trial of Plaintiff Barbara Earnest ("Plaintiff") is set to begin September 16, 2019.[2] At trial, Plaintiff intends to introduce the testimony of Dr. David Kessler. Dr. Kessler served as Commissioner of the FDA from 1990 to 1997. He has an M.D. from Harvard Medical School and a J.D. from the University of Chicago Law School. Defendants have filed the instant Motion seeking to limit his testimony.

LEGAL STANDARD

The admissibility of expert testimony is governed by Federal Rule of Evidence 702, which provides as follows:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
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> > (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
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> > (b) the testimony is based on sufficient facts or data;
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> > (c) the testimony is the product of reliable principles and methods; and
> >
> > (d) the expert has reliably applied the principles and methods to the facts of the case.[3]

The current version of Rule 702 reflects the Supreme Court's decisions in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*[4] and *Kumho Tire Co. v. Carmichael*.[5] The threshold inquiry in determining whether an individual may offer expert testimony under Rule 702 is whether the individual has the

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[2] To the extent the Motion relates to Plaintiff Tanya Francis, the Motion is moot, given the Court's dismissal of her case. *See* Doc. 7571. To the extent the Motion relates to Plaintiff Antoinette Durden, the same rulings issued herein apply to her case.
[3] FED. R. EVID. 702.
[4] 509 U.S. 579 (1993).
[5] 526 U.S. 137 (1999).

requisite qualifications.[6] After defining the permissible scope of the expert's testimony, a court next assesses whether the opinions are reliable and relevant.[7] As the "gatekeeper" of expert testimony, the trial court enjoys broad discretion in determining admissibility.[8]

First, to assess reliability, a court considers whether the reasoning or methodology underlying the expert's testimony is valid.[9] The party offering the testimony bears the burden of establishing its reliability by a preponderance of the evidence.[10] Courts should exclude testimony based merely on subjective belief or unsupported speculation.[11] Courts must, however, give proper deference to the traditional adversary system and the role of the jury within that system.[12] "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence."[13] After assessing reliability, a court evaluates relevance.[14] In doing so, a court must determine whether the expert's reasoning or methodology "fits" the facts of the case and will thereby assist the trier of fact in understanding the evidence.[15]

Federal Rule of Evidence 703 further provides that an expert may offer opinions based on otherwise inadmissible facts or data but only if (1) they are

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[6] Wagoner v. Exxon Mobil Corp., 813 F. Supp. 2d 771, 799 (E.D. La. 2011); *see also* Wilson v. Woods, 163 F.3d 935, 937 (5th Cir. 1999) ("A district court should refuse to allow an expert witness to testify if it finds that the witness is not qualified to testify in a particular field or on a given subject.").
[7] *See* United States v. Valencia, 600 F.3d 389, 424 (5th Cir. 2010). *See also* Wellogix, Inc. v. Accenture, L.L.P., 716 F.3d 867, 881–82 (5th Cir. 2013).
[8] *Wellogix*, 716 F.3d at 881.
[9] *See Daubert*, 509 U.S. at 592–93.
[10] *See* Moore v. Ashland Chem. Inc., 151 F.3d 269, 276 (5th Cir. 1998).
[11] *See Daubert*, 509 U.S. at 590.
[12] *See id.* at 596.
[13] *Id.*
[14] Burst v. Shell Oil Co., 120 F. Supp. 3d 547, 551 (E.D. La. 2015).
[15] *Id.*

of the kind reasonably relied upon by experts in the particular field; and (2) the testimony's probative value substantially outweighs its prejudicial effect.[16]

LAW AND ANALYSIS

In the instant Motion, Defendants raise several arguments relating to Dr. Kessler's testimony that as early as 2009 Sanofi had "reasonable evidence of a causal association" between Taxotere and irreversible alopecia. This "causal association" language stems from the FDA regulations, which provide that a drug's label "must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug."[17] Notably, the regulations further state that "a causal relationship need not have been definitely established."[18]

Defendants' first concern is that the jury will confuse "reasonable evidence of a causal association" with medical or legal causation. Defendants further argue that any testimony from Dr. Kessler on medical or legal causation would be inappropriate because Dr. Kessler did not apply a reliable methodology, such as the Bradford Hill factors, to form an opinion on medical or legal causation.[19] Defendants emphasize that "reasonable evidence of a causal association" is a lower threshold of proof than that which is required by state tort law to establish causation.

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[16] FED. R. EVID. 703.
[17] 21 C.F.R. § 201.57 (c)(6)(i).
[18] *Id.*
[19] General causation experts often rely on the Bradford Hill criteria, which derive from a 1965 lecture by a British epidemiologist and statistician, Sir Austin Bradford Hill. *See* In re Mirena Ius Levonorgestrel-Related Prods. Liab. Litig. (No. II), 341 F. Supp. 3d 213, 242 (S.D.N.Y. 2018). In the lecture, he identified nine criteria that can aid researchers in deciding whether a reported association in an epidemiological study reflects a truly causal relationship. *See id.*

The Court first notes that Dr. Kessler is not offering any opinions on medical or legal causation. His opinions relate to Sanofi's duty to warn and its failure to do so. Dr. Kessler, therefore, did not need to rely on the Bradford Hill factors, which courts use to assess general causation.[20] As Defendants note, the FDA's test looks only for a "causal association," not necessarily a definite causal relationship, and the Bradford Hill factors are used *after* a statistical association is found "to determine whether [the] association reflects a truly causal relationship."[21] Dr. Kessler, therefore, did not need to apply the Bradford Hill factors to determine whether, under the FDA regulations, Sanofi had "reasonable evidence of a causal association" that required it to update Taxotere's label.

Using the experience that he gained as Commissioner of the FDA, Dr. Kessler considered the seven factors that the FDA uses in determining whether there is "reasonable evidence of a causal association." Because Dr. Kessler is qualified and used a reliable methodology in forming his opinion, which will help the jury decide whether Sanofi breached its duty to warn, the Court will not exclude his testimony on the basis that it may confuse the jury. On cross-examination, Defendants can make clear for the jury that "reasonable evidence of a causal association" is distinct from medical or legal causation.

Defendants next argue that Dr. Kessler should not be permitted to opine on whether there was reasonable evidence to warn of a risk of "irreversible alopecia" because (1) Dr. Kessler cannot define "irreversible alopecia" and (2) the evidence he identified did not reliably meet an acceptable definition of that risk. The Court can see that defining "irreversible alopecia" is a challenge. In

[20] *See, e.g.*, In re Lipitor (Atorvastatin Calcium) Mktg., Sales Practices & Prods. Liab., 174 F. Supp. 3d 911, 914–16 (explaining that to establish general causation, there must first be an association between exposure to a drug and a disease; then the Bradford Hill factors are used "to determine whether an association reflects a truly causal relationship").
[21] *Id.*

his report, however, Dr. Kessler, adequately articulated the definition he used and his support for it. He wrote that the medical literature generally defines the condition as the "complete loss of growth or partial regrowth at least 6 months after chemotherapy."[22] To the extent Defendants disagree with this definition or believe that Dr. Kessler's use of it tainted his analysis, Defendants can explore this on cross-examination. The inherent difficulty of defining "irreversible alopecia" is not a basis for excluding Dr. Kessler's opinion.

Defendants next argue that Dr. Kessler's opinion is unreliable because it relies on data that did not exist in 2009. Defendants argue that in applying the seven factors set forth in the FDA regulations, Dr. Kessler finds support in analyses and articles dated after 2009. The Court finds that Dr. Kessler cannot rely on post-2009 data to support his opinion that Sanofi should have updated its label in 2009. Plaintiff notes that Dr. Kessler studied materials covering a range of years in an effort to determine whether and when a "causal association" developed. Even so, this does not mean that Dr. Kessler can rely on this broad array of materials in support of his tailored opinion about what Sanofi should have done in 2009. This opinion must be supported by information that Sanofi could have known in 2009.

However, the fact that Dr. Kessler considered, for example, Sanofi's 2015 Causation Analysis does not mean that the data he pulled from the analysis was from 2015. Sanofi's 2015 Causation Analysis included an examination of Sanofi's TAX 316 and GEICAM 9805 clinical studies, which collected data in 2004 and in 2009. Dr. Kessler writes that "Sanofi's 2015 Causation analysis cited to these clinical trial studies and the reports of irreversible alopecia reported to support its conclusion that 'the cumulative weighted evidence is

[22] Doc. 6146-7 at 24.

sufficient to support a causal association between docetaxel and permanent/irreversible alopecia in the patients who received docetaxel.'"[23] Accordingly, Dr. Kessler may rely on sources published or created after 2009 provided that the particular information he references is from 2009 or before.

Defendants further argue that Dr. Kessler should not be allowed to "parrot" the opinions of Dr. David Madigan. Defendants cite case law excluding opinions where an expert did "no original analysis" or where an expert gave "unblinking reliance" to another expert's opinion.[24] The instant case, however, presents distinguishable circumstances. Dr. Kessler gave enough consideration to Dr. Madigan's methodology,[25] and he did more than "parrot" Dr. Madigan's opinion. Dr. Kessler considered the seven factors that the FDA uses in determining whether there is "reasonable evidence of a causal association." His opinion, therefore, expanded on the opinion of Dr. Madigan, who provided statistical analyses at Dr. Kessler's request to assist with certain factors. This kind of collaboration is permissible under Rule 703:

> Federal Rule of Evidence 703 allows experts to base their opinions on facts or data that the expert has been made aware of or personally observed, which includes the efforts of other experts, provided that "experts in the particular field would reasonably rely on those kinds of facts or data in forming an opinion on the subject."[26]

The Court, therefore, will not exclude Dr. Kessler's opinion because he relied in part on Dr. Madigan's work.[27]

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[23] *Id.* at 46–47.
[24] Doc. 6146 at 14.
[25] *See, e.g.*, 6146-7 at 44 (explaining the methodology Dr. Madigan used in his search of the FDA's Adverse Event Reporting System ("FAERS")).
[26] Tajonera v. Black Elk Energy Offshore Operations, LLC, 2016 WL 3180776, at *10 (E.D. La. June 7, 2016).
[27] *See* In re Actos (Pioglitazone) Prods. Liab. Litig., 2014 WL 120973 at * 17 (W.D. La. Jan. 10, 2014) ("The Defendants do not challenge Dr. Kessler's epidemiological conclusions, rather, question his ability to discuss the fact that he relied on Dr. Madigan's meta-analysis

In a footnote, Defendants write that Dr. Kessler "vacillated about when the evidence became enough to change the label." Defendants note that Dr. Kessler identified a safety signal as early as 2004, that he said there was sufficient evidence in 2006, and that he said Dr. Madigan found a safety signal in 2000.[28] First, the Court is not convinced that these statements show "vacillation" by Dr. Kessler. Even if they do, however, *Daubert* does not require the certainty or precision that Defendants suggest it does.[29] As other courts have recognized, "[l]ack of certainty is not, for a qualified expert, the same thing as guesswork."[30] The Court, therefore, will not limit Dr. Kessler's testimony on the basis of "vacillation."

Defendants next argue that Dr. Kessler improperly characterizes irreversible alopecia as "serious" or "clinically significant," thereby warranting inclusion in the "Warnings and Precautions" section of Taxotere's label. In support of this argument, Sanofi quotes the FDA's "Guidance for Industry on Warnings and Precautions, Contraindications, and Boxed Warnings Sections of Labeling for Human Prescription Drug and Biological Products—Content and Format" (the "FDA Guidance"), which provides as follows:

> For example, non-serious adverse reactions (e.g., nausea, pruritus, alopecia) caused by drugs intended to treat minor, self-limiting conditions (e.g., allergic rhinitis, cosmetic conditions, transient insomnia) may be considered clinically significant. However, those same adverse reactions caused by drugs intended to treat serious or life-threatening conditions (e.g., cancer) may be considered

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in reaching his conclusions. It is without question, the facts and data upon which an expert may base his or her opinion(s) are admissible on that basis alone; Dr. Kessler needn't be a statistician to rely on statistics and analyses conducted by a statistician . . . .").

[28] A "safety signal" is "a concern about an excess of adverse events compared to what would be expected to be associated with a product's use." Doc. 6144 at 4 (quoting FDA materials).

[29] *See Daubert*, 509 U.S. at 590.

[30] Milward v. Acuity Specialty Prods. Grp., Inc., 639 F.3d 11, 22 (1st Cir. 2011) (quoting Primiano v. Cook, 598 F.3d 558, 565 (9th Cir. 2010)).

> much less clinically significant and not appropriate for inclusion in this section.

Defendants, therefore, assert that "Dr. Kessler came to a conclusion based on FDA Guidance when the FDA Guidance itself comes to the opposite conclusion."[31] But Defendants extrapolate too far from what the FDA Guidance states. The FDA Guidance does not contemplate permanent or irreversible alopecia just as it does not contemplate permanent nausea. The permanency of an adverse reaction may very well change its classification. Further, the FDA Guidance leaves room for discretion, saying that those "same adverse reactions caused by drugs intended to treat serious or life-threatening conditions (e.g., cancer) *may* be considered much less clinically significant and not appropriate for inclusion in this section." The FDA Guidance is not nearly as black-and-white as Defendants suggest. For these reasons, Dr. Kessler does not contradict the FDA Guidance.

Dr. Kessler devotes ten pages of his report to providing support for his conclusion that irreversible alopecia can be considered "serious" or "clinically significant."[32] He notes that under 21 C.F.R. § 314.80 a "serious adverse drug experience" includes "a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions."[33] He quotes the FDA Guidance stating that "[a]dverse reactions that do not meet the definition of a serious adverse reaction, but are otherwise clinically significant because they have implications for prescribing decisions or patient management, should also be included in the WARNINGS AND PRECAUTIONS section."[34] Citing the FDA Guidance, he writes that an adverse reaction can be considered clinically

[31] Doc. 6146 at 17.
[32] Doc. 6146-7 at 25–35.
[33] *Id.* at 26.
[34] *Id.*

significant if it "significantly affect[s] patient compliance, particularly when noncompliance has potentially serious consequences."[35] Dr. Kessler then examined several sources supporting the notion that a risk of irreversible alopecia affects patients compliance.[36]

The Court, therefore, rejects Defendants' argument that Dr. Kessler has no basis for considering irreversible alopecia to be "serious" or "clinically significant." The Court will not exclude Dr. Kessler's testimony based on Sanofi's interpretation of the FDA Guidance. To the extent Defendants believe that Dr. Kessler runs afoul of the FDA Guidance, Defendants can illuminate this for the jury on cross-examination.

Lastly, Defendants vaguely argue that the Court should exclude testimony from Dr. Kessler on (1) the intent, motive, state of mind, or knowledge of Sanofi or other entities, including "interpretation" of documents authored by Sanofi or other entities as a basis for such testimony; (2) testimony that merely repeats fact witness testimony or other written evidence; and (3) testimony containing legal conclusions. Defendants raise these same general arguments in its Motion to Preclude Improper Testimony. The Court declines to rule on these in the abstract and will revisit the arguments if and when Defendants tie their arguments to specific testimony.

CONCLUSION

For the foregoing reasons, **IT IS ORDERED** that Defendants' Motion to Exclude Expert Testimony of David A. Kessler, M.D., J.D. (Doc. 6146) is **GRANTED IN PART**, **DENIED IN PART**, and **DEFERRED IN PART**. In opining that Sanofi had "reasonable evidence of a causal association" as early

[35] *Id.*
[36] *Id.* at 27–33.

as 2009, Dr. Kessler is limited to relying on data from 2009 or before, as explained in this opinion.

New Orleans, Louisiana this 3rd day of September, 2019.

JANE TRICHE MILAZZO
UNITED STATES DISTRICT JUDGE